Renewable and Sustainable Energy Reviews 14 (2010) 2161–2166

Contents lists available at ScienceDirect

Renewable and Sustainable Energy Reviews

journal homepage: www.elsevier.com/locate/rser

Light-emitting diodes—Their potential in biomedical applications

Naichia Gary Yeh [a], Chia-Hao Wu [a], Ta Chih Cheng [b,*]

[a] College of Applied Sciences, MingDao University, 369 Wen-Hua Road, Peetou, Changhua 52345, Taiwan, ROC
[b] Department of Tropical Agriculture and International Cooperation, National Pingtung University of Science and Technology, 1 Hseuh-Fu Rd., Nei-Pu Hsiang, Pingtung 91201, Taiwan, ROC

ARTICLE INFO

Article history:
Received 19 January 2010
Accepted 17 February 2010

Keywords:
LED
Medical treatment
Phototherapy

ABSTRACT

The rapid development of high brightness light-emitting diodes (LEDs) makes feasible the use of LEDs, among other light sources (such as laser, intense pulse light and other incoherent light systems), for medical treatment and light therapy. This paper provides a general review on red, green, blue, ultraviolet LED applications in photo rejuvenation and medical treatments of a variety of physical abnormalities, as well as the relief of stress, circadian rhythm disorders, and seasonal affective disorder. The review, concentrated in the papers published after 1990, intends to show that LEDs are well qualified to succeed its more energy demanding counterparts in the named areas and beyond.

Contents

1. Introduction

LEDs, following laser and intense pulsed light (IPL), have become the new favorite in the field of medical treatment and phototherapy. Today, LEDs not only thrive in the field of low intensity photo rejuvenation; but are also used for the treatments of rhinitis, arthritis, jaundice, joint/tissue inflammation, skin abnormality, and for the relief of stress, seasonal affective disorder, as well as biological clock disorders.

LEDs are solid-state semiconductor devices which contain a single p–n junction, that is, the junction of a p-type layer where the carriers are positively charged holes and an n-type layer in which current is carried by mobile electrons.

LEDs pass an electrical current in the direction where electrons move from the n-region to the p-region. The electrons then recombine with holes to generate photons of light. The light emitted by a LED is usually in a narrow band of wavelength corresponding to the energy associated with electron–hole pair recombination. That energy is approximately the band gap energy of the semiconductor in which the recombination occurs.

As the performance of LED continues to improve ever since 1980s, these lighting systems progress from red-only LED arrays to high density, multi-color LED chip-on-board technologies. After the development of blue–green LEDs based on aluminum gallium indium nitride (AlGaInN) in the early 1990s, low-voltage light sources in all three primary colors (red, green and blue) have become available for the lighting and display industries. This development has also helped to penetrate multi-billion dollar markets in indoor agricultural production as well as medical treatment and phototherapy.

* Corresponding author. Tel.: +886 8 770 3202x6423; fax: +886 8 774 0446.
E-mail address: cheng.tachih@gmail.com (T.C. Cheng).

1364-0321/$ – see front matter
doi:10.1016/j.rser.2010.02.015

LEDs are the first light source to provide the capability of true spectral composition control, which allows wavelengths to match the requirement of the medical treatment to optimize the effectiveness. They are compact and have little difficulty reaching those hard to reach area. They are also easy to maneuver in small spaces. LED can be easily integrated into digital control systems to facilitate complex lighting programs like varying spectral composition over the course of a phototherapy or treatment stage. LEDs are safer to operate than current laser light sources as they do not need a high voltage power supply as sometimes required in laser-base medical system.

Following the previous review [1] of researches that use LEDs to support plant growth in controlled environments, this paper provides a general review on LED applications in a variety of medical treatment and phototherapy areas since 1990 to demonstrate the potential of LEDs in biomedical field.

2. LEDs for phototherapy and medical treatment

In order to establish a consensus that LED can be a safe and effective alternative to incoherent lights and laser (or other coherent lights) for photo rejuvenation and a variety of medical treatments, this research explores the papers that discuss such treatments using either conventional light sources or LEDs.

2.1. Relief for disorder and stress

Delayed sleep-phase disorder is a type of circadian rhythm disorder that affects the timing of sleep. Patients with such disorder have difficulty sleeping and waking at the times required for normal functions. This disorder is often related to change in geographical location and night activity. People with such disorder tend to fall asleep some hours after midnight and have difficulty waking up in the morning. Seasonal affective disorder (SAD) is another common type of circadian rhythm disorder, which is characterized by symptoms such as depression during the seasons when the duration of daylight is reduced. People who suffer from SAD usually have normal mental health but tend to experience fatigue, irritability, anxiety, social withdrawal, and a lack of alertness in the seasons with less sunlight. SAD is usually treated with light therapy where patients spend time before a set of bright lights to trick their brain into believing that the days are bright. A research conducted by Lewy et al. [2] has tracked sleep, activity levels, melatonin rhythms and depression symptoms of 68 SAD patients who took either low doses of melatonin or a placebo in the morning or afternoon for a winter month. The study shows that a person's rhythms are synchronized when the interval between the time the pineal gland begins to secret melatonin and the middle of sleep is about 6 h. These researchers propose that most patients will respond best to a low dose of the light-sensitive hormone melatonin in the afternoon in addition to 30 min of bright light in the morning. Without determining an optimal wavelength combination for SAD treatment, they suggest that clinical benefit of light treatment is greater than melatonin treatment.

Glickman et al. [3] have found that short wavelength light, especially blue light, demonstrates positive influence for acute melatonin suppression and circadian phase shifting. They have conducted light therapy on SAD patients using blue LEDs (468 nm at 607 $\mu W/cm^2$, 27 nm half-peak bandwidth) and dim red LEDs (654 nm at 34 $\mu W/cm^2$, 21 nm half-peak bandwidth). Twenty-four patients each receive 45 min of morning light treatment daily for 3 weeks. This research has demonstrated that blue light outperforms dimmer red light in reversing SAD symptoms.

2.2. Wound healing

Photobiomodulation, also known as low level light therapy (LLLT), is a medical technique in which exposures to low level laser light or LEDs stimulate cellular function leading to beneficial clinical effects. LLLT with light in the red to the near infrared range (630–1000 nm) has been shown to accelerate wound healing, improve recovery from ischemic injury, and attenuate degeneration in the injured optic nerve. Low fluence of photo irradiation at the cellular level can generate significant biological effects including cellular proliferation and the release of growth factors from cells.

Corazza et al. [4] have compared the blood vessels proliferation effects of laser and LEDs illumination on wounds induced in rats. The results have shown that the proliferations of blood vessels in all irradiated groups are superior in comparison to those of the control group, which indicates that both LED- and laser-based LLLT have demonstrated expressive results in angiogenesis.

With the inexpensive and easy-to-use LED light sources available, Erdle et al. [5] have evaluated the wound healing effect of 670-nm LED light on incisions and burn injuries in hairless mice and suggested that red light exposure may be helpful in postoperative wound repair. Their results show that while not so effective for burn injuries, 670-nm LED red light sources do accelerate healing in skin of hairless mice with incisions.

Whelan et al. [6] have used the LED originally developed for NASA plant growth experiments in space to access the effects of near infrared light treatment on wounds in a genetically diabetic mouse model and have found that certain tissue regenerating genes are significantly up regulated upon LED treatment. In a research that assesses the effects of hyperbaric oxygen and near infrared light therapy on wound healing, Whelan et al. [7] have also conducted *in vitro* and *in vivo* studies using a variety of LED wavelength, power intensity, and energy density parameters to identify conditions optimal for biostimulation. The results of theses two studies suggest that using LEDs for light therapy alone and in conjunction with hyperbaric oxygen greatly enhance the natural wound healing process, and more quickly return the patient to a pre-injury or pre-illness level. In a later research, Whelan et al. [8] have demonstrated that near infrared LED (670 nm @ 4 J/cm^2) treatment heals poisoned neurons by stimulating cytochrome oxidase activity, protects against retinal damage and improves the recovery of retinal function in a rodent model of mitochondrial poison-induced blindness; and promotes retinal healing and improved visual function following high-intensity laser-induced retinal injury in adult non-human primates. Both the experimental and clinical studies have found no evidence of damage to the retina or optic nerve following the LED treatment. As a result, they propose that near infrared LED photobiomodulation represents an innovative and non-invasive therapeutic approach for the treatment of retinal injury and disease.

Desmet et al. [9] have also studied the use of near infrared light treatment in various *in vitro* and *in vivo* models to determine the effect of near infrared LED light treatment on physiologic and pathologic processes. Their research found that the light treatment (1) stimulates the photoacceptor cytochrome oxidase, which results in increased energy metabolism and production, (2) accelerates wound healing in ischemic rat and murine diabetic wound healing models, (3) attenuates the retinotoxic effects of methanol-derived formic acid in rat models and the developmental toxicity of dioxin in chicken embryos, and (4) prevents the development of oral mucositis in pediatric bone marrow transplant patients. The experimental results demonstrate that near infrared LED light treatment stimulates mitochondrial oxidative metabolism *in vitro*, and accelerates cell and tissue repair *in vivo*.

Trelles and Allone [10] have studied 10 subjects regarding the effects of a LED phototherapy system on enhancing wound healing following the combination of eyelid surgery and laser ablative resurfacing. After the surgery, one-half of each subject's face was treated with the red LED therapy (20 min, 96 J/cm^2, 633 nm), the other half of each subject's face being the un-irradiated control. Erythema, edema, bruising, and days to healing were independently evaluated from the clinical photography. The 633 nm LED therapy-treated side is superior to the un-irradiated control by a factor of two to three in all instances.

Agnol et al. [11] have compared the wound healing effect of lights using LED and laser. They have established surgical dorsum lesions on 36 rats. For those subjects that have been irradiated once with LED (640 with 40 nm full bandwidth at half maximum) or laser (660 nm) 30 min after the establishment of the lesion, the researchers have found that the two light sources produced similar effects during a period of 168 h after the establishment of the lesion. For the group consisting of diabetic animals, 72 h after creation of the lesion, the therapy with LEDs had been more efficient than that with the laser in wound reduction.

The results of all these researches indicate that LED, a more economical low density light source, is a great alternative to laser for LLLT.

2.3. Treatment of acne vulgaris

Sun exposure has a beneficial effect on acne vulgaris (commonly called acne) but how wavelengths of the sun contribute to such effect is not clear. Lights in red, blue, green, violet, and ultraviolet segments have all been reported to be effective for the treatment of acne. The following researches have been conducted to define the most effective wavelengths.

Sigurdsson et al. [12] have treated 30 patients with mild to moderate facial, back, or chest acne vulgaris using three (full spectrum, green, and violet) light sources. Each patient receives a 20-min session light treatment three times a week for 7 weeks. The results show that the improvements by full spectrum, green, and violet are 14%, 22%, and 30%, respectively. While it seems that violet light is better than the other light qualities, the improvements induced by the three light sources have shown no statistically significant difference.

Papageorgiou et al. [13] have evaluated the effectiveness of blue light (peak at 415 nm) and a mixed blue and red light (peaks at 415 and 660 nm) in acne treatments. Their study randomly assigned 107 patients with mild to moderate acne in four treatment groups to be treated with blue light, mixed blue and red light, cool white light, and 5% benzoyl peroxide cream, respectively. Subjects in the phototherapy groups received irradiation 15 min daily from portable light sources. After 12 weeks of active treatment, the combined blue–red light group achieved a mean improvement of 76% in inflammatory lesions, significantly superior to that in all other groups. The final mean improvement by using blue–red light is 58%, still better than that in the other groups.

Although the acne treatment studies above have not indicated the light source used for their researches, yet there should be no significant down effect if the laser or any other light source in the treatment device is replaced with LEDs of the same frequencies according to the study of Lee et al. [14] These researchers have investigated the effectiveness of combined blue and red LEDs phototherapy for acne. They treated 24 patients with mild to moderate facial acne with alternating blue (415 nm) and red (633 nm) LED devices twice a week for 4 weeks. The study results indicate that the percentage improvements in non-inflammatory and inflammatory lesions have been 34.28% and 77.93%, respectively. Fourteen patients have reported brightened skin tone and improved skin texture. These studies basically conclude that phototherapy with mixed blue–red light, probably by combining antibacterial and anti-inflammatory action, is a safe, effective, and non-painful treatment for mild to moderate acne vulgaris, with no significant short-term adverse effects.

2.4. Photo rejuvenation

Over time, skin gradually displays the effects of aging. The collagen in the skin begins to break down and results in fine lines and then deeper grooves on the skin surface. Factors like sun, gravity, and hormones can speed up the aging process. The treatment of aging skin has always been a very popular topic. People who have skin conditions like flushed faces, sun-damaged skin, hyperpigmentation, enlarged pores may seek for the help of cosmetic surgery procedures, including photo rejuvenation. Increasing insight into the overlap between UV-induced skin cancer and UV-induced skin aging has contributed to the development of photoaging research. And market pressures have made photoaging research a prevailing field in investigative dermatology.

Both ablative and non-ablative resurfacing have been reported as solutions to intrinsic and photoaging and as being able to generate a younger dermal matrix. Non-ablative lasers and the IPL systems are aimed to avoid the undesirable development (such as pain, bruising, and redness) following laser ablative resurfacing, but these systems are still quite expensive and therapist-intensive. As a result the patient responses have been unsatisfactory.

Trelles et al. [15] suggest that no single modality can accomplish all the complex events required for effective skin rejuvenation. The combination phototherapy that uses different modalities in various combinations at sub-ablative thresholds should have better results. Therefore, the entry of blue and infrared tunable plasma light and LEDs into the skin rejuvenation arena has attracted attention.Lubart et al. [16] propose a photo rejuvenation mechanism based on light-induced reactive oxygen species (ROS) formation. They irradiate collagen *in vitro* with a broadband of visible light (400–800 nm, 24–72 J/cm^2) and have found that the irradiated collagen results in the formation of hydroxyl radicals. These researchers suggest that visible light at the energy doses used for skin rejuvenation (20–30 J/cm^2) produces high amounts of ROS, which destroy old collagen fibers, encouraging the formation of new ones. While at inner depths of the skin, where the light intensity is much weaker, low amounts of ROS are formed, which are well known to stimulate fibroblast production.

Trelles [17] have suggested that LED therapy represents a potential approach in anti-aging prevention. He has proposed to apply prevention to subjects in their very early 20 s before the appearance of fine lines. The prevention can be achieved via irradiating low level photo energy with specific wavelengths that, based on the photobiological findings, can stimulate both epidermal and dermal cells. He has also reported that the LEDs from the NASA Space Medicine Program can enhance action potentials of the skin cells and increases in local blood and lymphatic flow in a non-invasive, athermal manner. His conclusion is that LED-based systems can be less-expensive but clinically useful light source against photoaging.

3. Other biomedical applications

LED-based biomedical systems are also proved to be effective in the areas, which are described as follows:

Actinic keratosis: Actinic keratosis (AK), or solar keratosis, is a precancerous condition of thick, scaly, or crusty patches of skin associated with those who are frequently exposed to the sun. Babilas et al. [18] have conducted a controlled split-face study to evaluate the LED-based photodynamic therapy (PDT). They have

administered topical PDT to 17 patients whose AK is symmetrically distributed and suitable for a two-side comparison. After a necessary pretreatment, the AK is irradiated with incoherent lamp (160 mW/cm^2; 100 J/cm^2) on one side and LEDs (120 mW/cm^2; 40 J/cm^2) on the other. The results, after up to 6 months of follow-up evaluation, show that the AK reduction rates via both treatments have no significant difference (78.5% for LED vs. 80.3% for incoherent lamp). Also, there has not been significant difference between both treatments regarding the pain, cosmetic results, and patient satisfaction. The research suggests that LED-based PDT is a safe and effective alternative to incoherent light systems for the treatment of atinic keratoses.

Allergic rhinitis: Neuman and Finkelstein [19] have assessed the therapeutic effect of low-energy narrow-band red light (660 nm) phototherapy on nasal clinical symptoms of allergic rhinitis in a double-blind randomized prospective study. After reviewing the effectiveness of diode laser illumination, these researchers decided to investigate the effects of a 660-nm LED on patients with allergic rhinitis and nasal polyposis. Fifty allergic rhinitis patients received intranasal illumination for 4.4 min three times a day (total dose 6 J/day) for 14 days. Twenty-nine rhinitis patients received equivalent sham illumination as placebo. As compared with 24% in the placebo group, 72% of the allergic rhinitis patients have reported improvement of symptoms following the treatment. The differences have been significant. Same treatment has been applied to 10 nasal polyposis patients but no improvement was obtained in any of the patients. The study have lead to a conclusion that allergic rhinitis not complicated by polyps or chronic sinusitis can be effectively treated by narrow-band red light illumination of the nasal mucosa at 660 nm.

Anti-inflammatory: Inhibition of cyclooxygenase (COX) prostaglandin E_2 protects cells against cell injury in specific pathophysiological situations such as inflammation and oxidative stress. Some clinic studies report that irradiation of certain wavelength has anti-inflammatory effects during wound healing. Lim et al. [20] have investigated the anti-inflammatory mechanism of the red LED irradiation. The results show that 635 nm irradiation inhibits the expression of COX and prostaglandin E_2 releases and appears to be useful as an anti-inflammatory tool.

Dental application: The clinical performance of light polymerized dental composites is greatly influenced by the quality of the light-curing unit (LCU) used. The light outputs of halogen LCUs decrease with time. This may result in low degree of monomer conversion of the composites. The irradiance of LED LCUs is relatively low, yet their efficiency is close to that of the halogen LCUs of twice the irradiance. Studies have shown that blue light LED LCUs tend to polymerize dental composites without the above light decreasing drawbacks. Stahl et al. [21] have investigated the flexural properties of three different composites with three different shades, which were polymerized with either a commercial halogen LCU or an LED LCU, respectively. In most cases there have not been any significant differences in flexural strength and modulus between composites polymerized with the two kinds of LCUs.

Jaundice newborns: Newborn jaundice is a yellowing of the skin and other tissues of a newborn infant. Cremer et al. [22] first demonstrated that such symptom of some new born infants could be reduced by exposure to sunlight or artificial blue light. Lucey et al. [23] conducted a controlled clinical experiment among 111 premature infants to test the effectiveness of artificial light in preventing newborn jaundice. The control and treated groups were comparable regarding birth weight, gestational age, fluid intake, and weight loss. Infants, from 12 to 144 h of age, who need the treatment were placed in full spectrum light or blue light (450 nm) for an 8-day treatment. The results show a statistically significant difference between the control (58 infants) and treated (53 infants) groups. The study conducted in the incubators that consist of some daylight bulbs indicates that light treatment is a safe and simple method ideal for elimination of bilirubin in the newborn infant. Vreman et al. [24] have patented a phototherapy garment containing surface-mounted LEDs suitable for the treatment of newborn jaundice. The LEDs are arranged in a densely packed array facing the liner and emit uniform, high-intensity light. An infant who needs phototherapy can be placed inside the garment to receive uniform high-intensity blue light on a large portion of the skin. Thanks to LEDs, the size of treatment device of newborn jaundice has gone from a sizable incubator to a cozy wrap-around garment.

Mucositis: Mucositis, a dose-limiting complication of cancer treatment, may disturb treatment plan and can lead to serious, and sometimes, life threatening consequences. Low level lasers have been used for oral mucositis prevention and management with good results. Lang-Bicudo et al. [25] have evaluated the effectiveness of oral mucositis prevention in a cancer patient via phototherapy using LEDs. In their study, a 34-year-old man received intraoral irradiation with an infrared LED array (880 nm, 3.6 J/cm^2, 74 mW) for 5 consecutive days starting on chemotherapy day 1. The patient has not developed any oral mucositis during the five chemotherapy cycles and has had no pain symptoms. This result indicates that LED therapy is a safe and effective method for oral mucositis prevention.

Rheumatoid arthritis: McDonald [26] has conducted a study in which she instructed 60 female rheumatoid arthritis patients to place their hands into a box to be exposed in blue light for up to 15 min. Most subjects have experienced a pain relief after the exposure. McDonald has concluded that the pain relief is due to the blue light and the length of time exposed. The longer the exposure is, the greater the chance of pain relief. While the light source used in this 1982 study is not specified, there is no reason to rule out that blue light LED will have similar treatment effect. Hart and Malak [27] have patented a therapeutic light source for the treatment of arthritis or joint inflammation. The device includes a set of 350 to 1000 nm LEDs and fiber optic connections for treating and reducing inflammation and edema both internal and external, to joints, muscles, nerves, and skin tissues of the subject. The device can be worn in contact with the skin and surrounding the areas of inflammation, edema, neural, and muscular damage over short and long periods of time.

Venous ulcer: Caetano et al. [28] have used a randomized placebo-controlled double-blind study to compare a total of 20 patients divided into three groups to test the hypothesis that LED phototherapy with combined 660- and 890-nm light will promote healing of venous. The study has confirmed that phototherapy promotes healing of chronic venous ulcers, particularly large recalcitrant ulcers that do not respond to conventional treatment.

Other areas: Whelan et al. [29] have used LEDs with light-activated chemotherapeutic drugs to support that LED-technology is biologically optimal for PDT of cancer. These researchers reported that LED-technology developed for NASA plant growth experiments in space shows promise for delivering light deep into tissues to promote wound healing and tissue growth. The light therapy using these NASA LEDs significantly improves the medical care for astronauts on space missions. They also present the results of LED treatment of cells grown in culture and the effects of LEDs on patients' chronic and acute wounds. Their researches have other contributions that include (1) improving wound healing in laboratory animals by using LED light along with high-pressure oxygen; (2) improving over 40% in human musculoskeletal training injuries and decreasing wound healing time; (3) increasing *in vitro* animal cell growth to 140–200%; (4) increasing normal human epithelial cells growth to 155–171%; (5) producing a 47% pain reduction in children suffering from oral mucositis; and (6)

Table 1
Some common types of LEDs (as compiled from [1,32–34]) and their potential use for medical treatments.

Color	Peak wavelength (nm)	Material and structure	Substrate	Suitable for
Infrared	>760	GaAs, AlGaAs	–	Oral mucositis prevention and management (880 mm) [25]
Far red/near infrared	730	GaAs	GaP	Mucositis prevention, wound healing, and tissue repair [9]
Red	700	GaP:Zn–O	GaP	Low level light therapy (630–1000 mm) [4]
Red	~660	$GaAl_{0.35}As_{0.65}$	GaAs	Allergic rhinitis treatment [20], incision recovering [11], venous ulcer treatment [28], wound healing [8]
Red	~650	$GaAs_{0.6}P_{0.4}$	GaAs	Wound healing [11]
Orange-red	~630	$GaAs_{0.35}P_{0.65}$:N	GaP	Acne treatment [14], anti-inflammatory/wound healing [10,21]
Orange	~610	$GaAs_{0.25}P_{0.75}$:N	GaP	–
Yellow-orange	590–610	AlGaInP	GaP	–
Yellow	~590	$GaAs_{0.15}P_{0.85}$:N	GaP	–
Yellow	~585	$GaAs_{0.14}P_{0.86}$:N	GaAs	–
Yellow	570–590	GaAsP, AlGaInP	GaP	–
Green	~565	GaP:N	GaP	–
Green	530–555	AlGaInN	GaN	–
Green	500–570	InGaN, AlGaInP, AlGaP	GaN	–
Blue	450–500	ZnSe, InGaN	SiC	Treatment of seasonal affective disorder [3],
Blue	~450	GaN	SiC	dental composite polymerization [22], treatment of rheumatoid arthritis [26,27]
Ultraviolet	~400	AlGaN	AlN	Water purification, biomedical researches [35–37]
Ultraviolet	210–400	AlGaInN	Diamond(C)	

quintupling DNA synthesis in fibroblasts and muscle cells in one application using the combination of 680, 730 and 880 nm LED.

4. Conclusion

Besides being used for the treatments of rhinitis, arthritis, jaundice, etc. LEDs are used for the relief of stress, seasonal affective disorder, and biological clock disorders; not to mention that LEDs are thriving in the field of low intensity photo rejuvenation. The LED-based PDT has even been expanded to cancer treatments [30].

LEDs allow the adjustment of light intensity. They have the ability to produce high light levels with low radiant heat output and maintain useful light output for years. LED-based systems can provide a homogenous light dose in optimal intensity. While lasers provide tissue stimulations which increase cellular activity during wound healing, they have limitation in wavelengths. It is difficult for lasers to produce the efficient wavelength combination optimal for wound healing. The size of wounds that may be treated by the small beam width of laser is also limited. In contrast, LEDs allow the control of spectral composition and can be arranged in flat arrays of all sizes for the treatment of small or large areas. LEDs offer an effective alternative to conventional light sources also for the following reasons:

1. Using LED array light source for medical devices is much more economical than using IPL or laser sources. LEDs are highly durable and thus are less-expensive in the long term. Their compact and light design and the resulting lower weight make the use of LED systems simpler.
2. Solid-state high efficiency LED is safer to use than the traditional gas laser. The energy level of LED is low. When used in medical treatment, LED-based systems do not need a high voltage power supply as required in laser-based ones. When required, LED-based devices are more easily to be made self-contained. They can be continuously operated with a battery pack for a longer period. For any medical treatment equipment, especially those used in the remote areas where no modern utilities are readily available, this is an attractive feature.
3. While many of the wavelength segments are not yet available in semiconductor laser, wavelengths generated from LEDs have covered partial ultraviolet, near infrared, and almost all the visible bands.
4. LEDs produce less heat than high-pressure lamps and thus the hyperthermic effects that can be induced by high-intensity light sources are avoided. As a result, LEDs can be placed in a closer range from the treatment areas than other light sources so there will be less distance to diminish the intensity required. This accounts for more energy saving.
5. Their relatively narrow emission spectrum of LED systems can be optimally tuned so as to correspond to the treatment requirement and thus eliminates wavelengths not needed for the therapy. As a result, the irradiation time required for treatment is much shorter than with incoherent light sources.

The studies reviewed in this paper indicate that LEDs have opened up new prospects as an effective light source of phototherapy and medical treatment as they have in indoor agriculture. One thing noteworthy is that the wavelengths proved to be effective are centralized in red, blue, and infrared segments (see Table 1) for both agricultural production and medical treatment. It is safe to say that the researches about the biomedical effect of other wavelengths (i.e. orange, yellow, and green) may lead to additional discoveries.

As the LED-manufacturing related patents issued since 1990 will expire starting from 2010 [31], LED-manufacturers who hold patents may expand their license deals with other companies to make full use of those patents before the expiration date. These manufacturers may also develop new patent technology to produce new products that can boost the LED industry. All these lead to lower LED costs and more LED varieties. Therefore, LED-based applications, along with phototherapy, are setting out for a superior outlook in the years to come as LED becomes more qualified to replace its more energy demanding counterparts.

Acknowledgement

This study is supported by grant from National Science Council of Taiwan under the contract No. NSC: 98-2313-B-451-001-MY3.

References

[1] Yeh N, Chung J-P. High-brightness LEDs—energy efficient lighting sources and their potential in indoor plant cultivation. Renew Sustain Energy Rev 2009;13:2175–80.
[2] Lewy AJ, Lefler BJ, Emens JS, Bauer VK. The circadian basis of winter depression. Proc Natl Acad Sci USA 2006;103(May):7414–9.

[3] Glickman GBB, Pineda C, Hauck WW, Brainard GC. Light therapy for seasonal affective disorder with blue narrow-band light-emitting diodes (LEDs). Biol Psychiatry 2006;59:502–7.
[4] Corazza AV, Jorge J, Kurachi C, Bagnato VS. Photobiomodulation on the angiogenesis of skin wounds in rats using different light sources. Photomed Laser Surg 2007;April (25):102–6.
[5] Erdle BJ, Brouxhon S, Kaplan M, Vanbuskirk J, Pentland AP. Effects of continuous-wave (670-nm) red light on wound healing. Dermatol Surg 2008;March (34):320–5.
[6] Whelan HT, Buchmann EV, Dhokalia A, Kane MP, Whelan NT, Wong-Riley MTT, et al. Effect of NASA light-emitting diode irradiation on molecular changes for wound healing in diabetic mice. J Clin Laser Med Surg 2003;21(April):67–74.
[7] Whelan HT, Smits Jr RL, Buchman EV, Whelan NT, Turner SG, Margolis DA, et al. Effect of NASA light-emitting diode irradiation on wound healing. J Clin Laser Med Surg 2001;19(December):305–14.
[8] Whelan HT, Wong-Riley MTT, Eells JT, VerHoeve JN, Das R, Jett M. DARPA soldier self care: rapid healing of laser eye injuries with light emitting diode technology. RTO MP HFM 2004;109:19–37.
[9] Desmet KD, Paz DA, Corry JJ, Eells JT, Wong-Riley MTT, et al. Clinical and experimental applications of NIR-LED photobiomodulation. Photomed Laser Surg 2006;24(Apr):121–8.
[10] Trelles MA, Allones I. Red light-emitting diode (LED) therapy accelerates wound healing post-blepharoplasty and periocular laser ablative resurfacing. J Cosmet Laser Ther 2006;8(April):39–42.
[11] Agnol MAD, Nicolau RA, Lima CJD, Munin E. Comparative analysis of coherent light action (laser) versus non-coherent light (light-emitting diode) for tissue repair in diabetic rats. Lasers Med Sci 2009.
[12] Sigurdsson V, Knulst AC, van Weelden H. Phototherapy of acne vulgaris with visible light. Dermatology 1997;194:256–60.
[13] Papageorgiou P, Katsambas A, Chu A. Phototherapy with blue (415 nm) and red (660 nm) light in the treatment of acne vulgaris. Br J Dermatol 2000;142(May):973–8.
[14] Lee SY, You CE, Park MY. Blue and red light combination LED phototherapy for acne vulgaris in patients with skin phototype IV. Lasers Surg Med 2007;39(February):180–8.
[15] Trelles MA, Mordon S, Calderhead RG. Facial rejuvenation and light: our personal experience. Lasers Med Sci 2007;22(June):93–9.
[16] Lubart R, Friedmann H, Lavie R, Longo L, Jacobi J, Baruchin O, et al. A reasonable mechanism for visible lightinduced skin rejuvenation. Lasers Med Sci 2007;22(March):1–3.
[17] Trelles MA. Phototherapy in anti-aging and its photobiologic basics: a new approach to skin rejuvenation. J Cosmet Dermatol 2006;5(March):87–91.
[18] Babilas PTR, Werner A, Landthaler M, Szeimies RM. Split-face-study using two different light sources for topical PDT of actinic keratoses: non-inferiority of the LED system. J Dtsch Dermatol Ges 2008;6(January (1)):25–32. Epub 2007 Nov. 9 English, German. PMID: 17995967 [PubMet-indexed for MEDLINE].
[19] Neuman I, Finkelstein Y. Narrow-band red light phototherapy in perennial allergic rhinitis and nasal polyposis. Ann Allergy Asthma Immunol 1997;78(April):399–406.
[20] Lim W, Lee S, Kim I, Chung M, Kim M, Lim H, et al. The anti-inflammatory mechanism of 635 nm lightemitting-diode irradiation compared with existing COX inhibitors. Lasers Surg Med 2007;3(August):614–21.
[21] Stahl F, Ashworth SH, Jandt KD, Mills RW. Light-emitting diode (LED) polymerisation of dental composites: flexural properties and polymerisation potential. Biomaterials 2000;21(July):1379–85.
[22] Cremer RJ, Perryman PW, Richards DH. Influence of light on the hyperbilirubinaemia of infants. Lancet 1958;1(May):1094–7.
[23] Lucey J, Ferriero M, Hewitt J. Prevention of hyperbilirubinemia of prematurity by phototherapy. Pediatrics 1968;41(June):1047–54.
[24] Vreman HJ, Seidman DS, Stevenson DK. Phototherapy of jaundiced newborns using garments containing semiconductor light-emitting devices, US Patent 6,596,016; 2003.
[25] Lang-Bicudo L, Eduardo Fde P, Eduardo Cde P, Zezell DM. LED phototherapy to prevent mucositis: a case report. Photomed Laser Surg 2008;26(December):609–13.
[26] McDonald SF. Effect of visible light waves on arthritis pain: a controlled study. Int J of Biosocial Research 1982;3(2):49–54.
[27] Hart, BM, Malak H. Joint/tissue inflammation therapy and monitoring device(s) JITMon device. US Patent no.: US20030167080A1; 2003.
[28] Caetano KS, Frade MA, Minatel DG, Santana LA, Enwemeka CS. Phototherapy improves healing of chronic venous ulcers. Photomed Laser Surg)2009;(January).
[29] Whelan HT, Buchmann EV, Whelan NT, Turner SG, Cevenini V, Stinson H, et al. NASA light emitting diode medical applications from deep space to deep sea. In: Space Technology and Applications International Forum-2001, vol. 552. 2001. p. 35–45.
[30] Araujo AHPC, Da Silva N, Moraes K. Cellular and molecular studies of the initial process of the photodynamic therapy in HEp-2 cells using LED light source and two different photosensitizers. Cell Biol Int 2009;33:785–95.
[31] LEDinside News, Many patents will expire in 2010, LED market would be reformed; 2008.
[32] Dumé B. LEDs move into the ultraviolet; 2006.
[33] Wetzel C, Detchprohm T, Hanser D, Preble E. Closing the "Green Gap" in LED materials. In: Presented in US DOE Solid Stante Lighting R&D Workshop; 2009.
[34] Nishida T, Ban T, Saito H, Makimoto T. High current injection to a UV-LED grown on a bulk AlN substrate. Mater Res Soc Symp Proc 2004;798.
[35] Kaidbey KH, Kligman AM. Sunburn protection by longwave ultraviolet radiation-induced pigmentation. Arch Dermatol 1978;114(January):46–8.
[36] Mills OH, Kligman AM. Ultraviolet phototherapy and photochemotherapy of acne vulgaris. Arch Dermatol 1978;114(February):221–3.
[37] Kaidbey KH, Kligman AM. The acute effects of long-wave ultraviolet radiation on human skin. J Invest Dermatol 1979;72(May):253–6.